amino acids 22-167 of SEQ ID NO: 4; and

e) a nucleic acid molecule which hybridizes under moderate stringency hybridization conditions to the polynucleotide of any one of a) through d). --

REMARKS

The foregoing amendments and the following remarks are submitted in response to the Office action mailed May 21, 1998.

The Examiner has objected to the specification at page 142, line 29 and at page 143, line 6 as lacking the specific SEQ ID NO. Applicants have amended the specification to incorporate the corresponding SEQ ID in the Specification as noted by the Examiner.

Status of the Claims

Claims 124 and 132-162 are pending in the application. Claims 124, 132-135, 138-149 and 154-159 have been amended and new Claims 163-164 are presented in order to more particularly point out and distinctly claim that which Applicants regard as the invention. Support for the amended claims can be found generally through Applicants' specification.

The Specification Fully Enables the Claimed Invention

The Examiner has rejected claim 124 and 132-162 under 35 U.S.C. 112, first paragraph, because the Examiner asserts that "the specification, while being enabling for the use of a gene encoding the mouse OB polypeptide as shown in SEQ ID NOS: 2, 4, 5 or 6 as well as any OB polypeptide thereof lacking the signal sequence of amino acids 1-21, for modulating the body weight of *ob/ob* mice or normal mice, does not reasonably provide enablement for using other variants (except natural alleles), muteins, analogs and fragments of these OB polypeptides, nor is the specification enabling for modulating the body weight of any other mammals, including humans". The Examiner points out two specific issues regarding enablement of the scope of the claims, each of which will be addressed by Applicants below.

The first issue presented by the Examiner regarding enablement involves the scope of the variants, muteins and analogs of the OB polypeptide embraced by the claims to have the ability to modify the body weight of a mammal. Applicants respectfully disagree and submit that the Specification provides sufficient guidance and a significant and representative number of such variants and analogs, capable of modulating body weight to enable the claimed genus of sequences encoding OB polypeptide.

Applicants first point out that Applicants have now amended Claims 124, 139, 145, and 155 to refer to "variants (including allelic variants), analogs and fragments". Applicants have chosen to cancel the term "mutein" from the claims in an effort to expedite issuance and in as much as the term is perceived to be redundant with the term "analog". In particular, at all points in the specification where the term "mutein" is recited, clear definitional association is present with regard to the term "analog". Thus, the term "analog" subsumes within its scope the term "mutein" as an example thereof.

The claims set out a particular group of variants and analogs, which are representative of the variants and analogs fully supported by the Specification, which are capable of modulating body weight. The skilled artisan could readily determine using standard and recognized methods, including those taught in the Specification, whether or not modulation had occurred, even if such modulation was slight or was some degree of weight change. It is well recognized that weight change in individuals can be (and usually is) brought about by gradual, but significant overall, changes in body weight. Even the relatively unskilled individual, or dieter, can recognize a change in weight when it occurs.

With regard to the Examiner's objection to the number of embodiments claimed, Applicants reiterate that the making and testing of any variant, analog or fragment within the scope of the claims is fully supported by the Specification. In addressing the number of variants and analogs claimed, the Examiner has directed Applicants to the findings of *The Regents of the University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC 1997), which, contrary to the Examiner's position, support Applicants' entitlement to the full scope of the claims. In particular, the CAFC found:

A description of a genus of cDNAs may be achieved by means of a recitation of a

representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus ... (emphasis added).

Applicants submit that the instant Application sets out a significant and representative number of nucleic acids encoding OB polypeptide analogs, which representative number constitutes description of the genus of specific nucleic acids which Applicants claim. In particular, as noted by the Examiner, the Specification provides the sequence of mouse and human OB polypeptide encoding nucleic acid and Figure 4 notes those cites where these encoded OB polypeptides differ. Taking encoded analogs at these 22 cites alone, the instant Application provides a representative number of nucleic acids encoding OB polypeptide analogs. For instance, in the event that only a swap is made of the mouse amino acid at any combination of these different cites (which is supported in the Specification including at Figure 4, and as discussed by the Examiner at page 5 of his response) a representation number of 2^{22} or 4,194,304 analogs are described. Exemplary of the genus which is claimed, the instant Application provides a significant and representative number of nucleic acids encoding OB polypeptide variants and analogs. The claims further require that any encoded variant or analog have a functional feature of being capable of modulating body weight, as outlined and demonstrated in the Specification.

The second issue presented by the Examiner regarding enablement is in regard to the scope of enablement for the methods which modify the body weight of a mammal. Applicants again submit that it would not constitute undue experimentation to make and test OB polypeptides for use in gene therapy methods of modifying body weight in humans. The skilled artisan, using diagnostic methods known in the art and the teaching in the Specification, including at page 65-69, to identify those individuals, including those with altered or unaltered levels or forms of OB polypeptide, which could reasonably be expected to benefit from the administration of the OB gene (or polypeptide) to modify body weight as claimed. It is reasonable to predict, given the teaching in the Specification and the knowledge and experience of the skilled artisan, that the administration of the OB gene (or polypeptide) could modify

body weight in humans.

The Examiner has rejected Claims 133, 141, 147 and 157 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the Examiner remarks that there is no support in the Specification for the percent homology. Applicants respectfully disagree and submit that percent homology is supported by the Specification, including in Figure 4, and that the skilled artisan could determine percent homology, using Figure 4, or his or her own knowledge and skill. Nonetheless, in order to expedite issuance, and without prejudice against the pursuit of any such claim language at a later date, Applicants have now amended Claims 133, 141, 147 and 157 to recite "83 percent or greater amino acid sequence identity". Even as noted by the Examiner at page 14 of his response, Figure 4 of the Specification provides specific demonstration of 83 percent identity in the comparison of the mouse and human OB polypeptide sequences.

With regard to Claims 161 and 162, the Examiner argues that the Specification fails to describe or teach how to make and/or use the invention claimed. Claim 161 claims methods of activating the expression of OB encoding nucleic acid by means of inserting an expression regulatory sequence in functional proximity to the OB polypeptide encoding sequence. Claim 162 claims methods of modifying body weight by administering mammalian cells comprising an OB polypeptide encoding sequence modified *in vitro* by such means. The skilled artisan could, implementing their knowledge and through the teaching in the Specification, practice such claimed methods and could insert an expression regulatory control sequence in functional proximity to OB polypeptide encoding sequence. *In vitro* modification is comparably more straightforward and could be accomplished, for instance, by insertion of an expression regulatory control sequence immediately upstream and adjacent to the initiation methionine disclosed in the sequences provided in the Specification using standard molecular biology techniques. Similarly, an expression regulatory control sequence could be inserted immediately upstream and adjacent to the initiation methionine by homologous recombination.

It is well within the capability of the skilled artisan to promote homologous recombination for insertion of an expression regulatory control sequence in functional proximity to OB polypeptide encoding sequence, using the disclosed sequences or on identifying additional resident OB sequences as necessary. The identification of any such additional resident OB sequences is well within the ability of the skilled artisan.

In view of the foregoing remarks, Applicants submit that the Examiner's rejection under 35 U.S.C. 112, first paragraph may properly be withdrawn.

Particularity and Distinctiveness of the Claims

The Examiner has rejected Claims 124, 133, 141, 147 and 157 under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter applicant regards as the invention.

With regard to Claim 124, the Examiner objects to the claim in that the method involves "administering a nucleic acid". Applicants have now amended claim 124, and the claims dependent on claim 124 which are now set out as independent claims, to refer to "administering to the mammal a vector comprising a nucleic acid molecule".

Regarding Claims 133, 141, 147 and 157, the Examiner objects to the term "homology". Applicants have now amended Claims 133, 141, 147 and 157 to recite "83 percent or greater amino acid sequence identity". Even as noted by the Examiner at page 14 of his response, Figure 4 of the Specification provides specific demonstration of 83 percent identity in the comparison of the mouse and human OB polypeptide sequences.

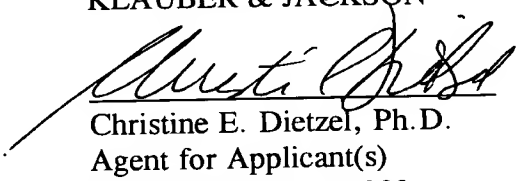
In view of the foregoing amendments and remarks, Applicants submit that the Examiner's rejection is obviated and should be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,

KLAUBER & JACKSON



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